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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,693	10/16/2001	Jonathan S. Stamler	Duke 1931	3762

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Ivor R. Elrifi, Esq.  
Mintz, Levin, Cohn, Ferris Glovsky and Popeo PC  
One Financial Center  
Boston, MA 02111

EXAMINER

SCHLAPKOHL, WALTER

ART UNIT PAPER NUMBER

1636

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/977,693	<b>Applicant(s)</b> STAMLER, JONATHAN S.	
	<b>Examiner</b> Walter Schlapkohl	<b>Art Unit</b> 1636	<i>huf</i>

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 August 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-9,11 and 12 is/are pending in the application.
- 4a) Of the above claim(s) 11 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3,5,6 and 9 is/are rejected.
- 7) ☒ Claim(s) 7 and 8 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

Receipt is acknowledged of the papers filed 8/30/2006 in which claims 1-2 & 5-6 were amended and claims 13-17 were cancelled. Claims 1-3, 5-9 and 11-12 are pending in the instant Application. Claims 11-12 are withdrawn. Claims 1-3 and 5-9 are under examination in the instant Office action.

***Claim Objections***

The objection to claim 1 is WITHDRAWN in view of Applicant's amendments to the claim.

The objection to claim 16 is rendered moot because claim 16 has been cancelled.

Claim 8 is objected to because of the following informalities: claim 8 recites "[t]he method of Claim 7 where the oxygen tensions employed are in step (b) range from 0.1 mm Hg to 145 mm Hg" in lines 1-2. Claim 8 should instead recite "[t]he method of Claim 7 where the oxygen tensions employed [[are]] in step (b) range from 0.1 mm Hg to 145 mm Hg."

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 2, 5-6 and 13-14, and therefore dependent claims 7-9 and 15-17, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention, is hereby WITHDRAWN in view of Applicant's amendments.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-3 and 5-9 under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement on the grounds that the phrase "wherein the plurality of proteins are screened concurrently" is new matter, is hereby WITHDRAWN in view of Applicant's arguments.

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The rejection of claims 13-17 under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement on the grounds that they comprise new matter, is hereby WITHDRAWN in view of Applicant's cancellation of the claims.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection. This is a new rejection necessitated by Applicant's amendment.**

The specification as originally filed does not provide support for the invention as now claimed: a method of establishing a protein-protein interaction map comprising (a) screening for a protein-protein interaction between at least one protein and a plurality of proteins, where the screening is performed in the absence and in the presence of a simulated redox state perturbation and wherein the redox state perturbation is generated by a process which includes an "alteration in NAD<sup>+</sup>/NADH ratio." The specification does not

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provide sufficient blazemarks nor direction for the methods encompassed by the above-mentioned limitation, as currently recited. Applicant asserts that support for the amendment can be found on page 4, lines 15-19. However, it is noted that page 4, lines 15-19 recite that "[r]edox state perturbations are caused for example, by redox state modifier molecules in concentration variation from physiological state, glucose concentration variation from physiological state and pH variation from physiological state as determined in affected tissue or cell or in blood perfusing affected tissue, or the presence of transition metal or other thiol chelating metal such as zinc or by alterations in any NADH ratio" (emphasis added). Thus, not only does the instant claim now recite a limitation, which was not clearly disclosed in the specification as filed, and which now changes the scope of the instant disclosure as filed; it provides support for Examiner's contention that the specification contemplates more than one type of NADH ratio and therefore that an alteration in an  $\text{NAD}^+/\text{NADH}$  ratio is new matter. Such a limitation recited in the present claims, which did not appear in the specification as filed, introduces new concepts and violates the description requirement of the first paragraph of 35 U.S.C. 112.

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***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 5-6 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Poellinger et al (US Patent Application Pub. US/2002/0048794 A1). **This is a new rejection not necessitated by Applicant's amendment.**

Poellinger et al teach a method of establishing a protein-protein interaction map comprising (a) screening for a protein-protein interaction between at least one protein and a plurality of proteins, where the screening is performed in the absence of a simulated redox state perturbation and where the plurality of proteins are screened concurrently; (b) screening for a protein-protein interaction between the at least one protein and a plurality of proteins, where the screening is performed in the

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presence of a simulated redox state perturbation and where the plurality of proteins are screened concurrently; and (c) generating the protein-protein interaction map by identifying at least one different protein-protein interaction between (a) and (b) (see entire document, especially paragraphs 138-140 and Figures 19 and 20). Specifically, Poellinger et al screen for a protein-protein interactions between the GAL4/HIF-1 $\alpha$  fusion protein and VHL and ARNT under normoxic and hypoxic conditions. The Western blots showing co-immunoprecipitation results as in Figures 19 and 20 are the "interaction map" and a noted difference in protein-protein interactions between (a) and (b) is, e.g., a difference in HIF-1 $\alpha$ 's ability to bind to Arnt and VHL under normoxic and hypoxic conditions. Regarding claim 6, the VHL gene is associated with von Hippel-Lindau (VHL) disease (see paragraph [0001]). Regarding claim 9, the results of the protein-protein interaction assay revealed that VHL is not released from HIF-1 $\alpha$  in hypoxic cells, i.e., under conditions similar to those found in VHL-associated neoplasms (ibid).

Claims 1-3 are rejected under 35 U.S.C. 102(a) as being anticipated by Dedio (*The FASEB Journal* 15(1):79-89, 2001).

**This is a new rejection not necessitated by Applicant's amendment.**



Dedio et al teach a method of establishing a protein-protein interaction map comprising (a) screening for a protein-protein interaction between at least one protein and a plurality of proteins, where the screening is performed in the absence of a simulated redox state perturbation and where the plurality of proteins are screened concurrently; (b) screening for a protein-protein interaction between the at least one protein and a plurality of proteins, where the screening is performed in the presence of a simulated redox state perturbation and where the plurality of proteins are screened concurrently; and (c) generating the protein-protein interaction map by identifying at least one different protein-protein interaction between (a) and (b) (see entire document, especially Figure 2 and page 83, first full paragraph). Specifically, Dedio et al teach a coimmunoprecipitation assay that shows interaction between eNOS and NOSIP but not between eNOS and GFP in the presence and absence of A23187 (see Figure 2B). Therefore Dedio et al teach the generation of a protein-protein interaction map between at least one protein (eNOS) and a plurality of proteins (NOSIP and GFP) in the presence and absence of a simulated redox state perturbation (addition of A23187 which activates NOS and thus increases nitric oxide), or, in other words, the variation of a redox state modifier molecule from physiological state.

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The rejection of claims 1-2, 5-6, 9 and 13-14 under 35 U.S.C. 102(b) as being anticipated by Tucci et al (*Journal of Endocrinology* 157:13-24, 1998) is hereby WITHDRAWN in view of Applicant's amendment and further in view of Applicant's arguments.

The rejection of claims 13-17 under 35 U.S.C. 102(e) as being anticipated by Loehrlein et al (Patent Application Publication No. US 2002/0160361) is hereby WITHDRAWN in view of Applicant's cancellation of the claims.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 1-3, 5-9 and 13-17 under 35 U.S.C. 103(a) as being unpatentable over Tucci et al (cited above) in view of Livingston et al (WO 00/74725 A1) is hereby WITHDRAWN in view of Applicant's amendments to the claims and further in view of Applicant's arguments.

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***Allowable Subject Matter***

Claims 7 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

No claim is allowed.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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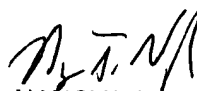
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Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Thursday from 8:30 AM to 6:00 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

Walter A. Schlapkohl, Ph.D.  
Patent Examiner  
Art Unit 1636

November 3, 2006

  
NANCY VOGEL  
PRIMARY EXAMINER